ATTORNEY DOCKET NO. 14014.0349U2
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	)	
	)	
Blackshear *et al.*	)	Group Art Unit: 1634
	)	
Application No. 10/049,586	)	Examiner: Sisson, B. L.
	)	
Filing Date: February 12, 2002	)	Confirmation No. 9700
	)	
For: TTP-RELATED ZINC FINGER DOMAINS AND METHODS OF USE	)	

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

NEEDLE & ROSENBERG, P.C.
Customer Number 36339

Sir:

I, Jack D. Keene, hereby declare that:

1. I am a James B. Duke Professor of Molecular Genetics and Microbiology and Director of the Center for RNA Biology at Duke University. I hold a Ph.D. in microbiology and immunology from University of Washington, Seattle and a B.A. from University of California, Riverside. I was trained in the molecular biology of RNA viruses as a Staff Fellow at the National Institutes of Health in Bethesda, Maryland. I have over 30 years experience in the field of RNA metabolism, with an emphasis on RNA-protein interactions, and over 25 years experience in the study of regulation of RNA by RNA-binding proteins. This includes specific experience in the study of the structure and function of RNA-binding proteins and their role in gene expression. A partial curriculum vitae is attached to this declaration as an exhibit.

2. I have reviewed the specification and the claims in the above-identified application. Specifically, I have reviewed page 30, beginning at line 8, wherein the Applicants disclose that

"[a] variety of assay methods can be used to determine whether a given compound interferes with TTP or related protein binding to the GM-CSF ARE and the breakdown of GM-CSF mRNA."

3. As an expert in the field of RNA metabolism in general and the study of regulation of RNA by RNA-binding proteins in particular, and as an individual with extensive knowledge of the level of understanding of those of skill in the art of RNA metabolism at the time Application Serial No.10/049,586 was filed, I believe that someone in the field of RNA metabolism at the time the application was filed would have been able to envision all of the steps of the recited methods for identifying a compound that interfered with the binding of TTP to an ARE based on the description provided in the specification.

4. Further, it is my opinion that the description of the assay methods that can be used in the provided methods is clear and straightforward. It is my opinion that a person in this field would have recognized phrases such as "would include," "could use," and "would probably be the most convenient" as a sufficiently affirmative and clear disclosure of the types of assay methods available to a practitioner at the time the application was filed to allow for the practice of the claimed method. Further, the example of the assay methods provided on pages 64-68 of the specification, in light of the specification as a whole, gives a clear indication of what the claimed methods are and how they are to be practiced.

5. I further believe that the asserted use of the claimed method, *i.e.*, for the identification of a compound that inhibits the degradation of GM-CSF mRNA that would be a candidate for use in a method of treating granulocytopenia in a subject, is a scientifically credible utility based on the data presented in the specification. For example, data are provided on pages 61-106 of the specification, such as for example page 100, lines 9-19, demonstrating the degradation of the

TNF-α mRNA ARE by TTP. Further, the data provided on page 38, lines 14-22, demonstrating the accumulation, prolonged expression, and lack of the deadenylated form of GM-CSF mRNA in TTP-deficient cells in response to stimulus, indicate the degredation of GM-CSF mRNA by TTP. These data, in view of the known role of GM-CSF in granulocytopenia (Nemunaitis J, Drugs. 1997 Nov;54(5):709-29, attached), provide a clear and credible indication that an inhibitor of GM-CSF mRNA degradation could be identified for use in treating granulocytopenia.

6. All statements made herein of my own knowledge and belief are true and that all statements made on information and belief are believed to be true, and further, that the statements are made with the knowledge that willful false statements are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: 8/22/05

Jack D. Keene